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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/812,884	03/21/2001	Russell John Mumper	50229-262	1135

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EXAMINER	
YOUNG, MICAH PAUL	

ART UNIT	PAPER NUMBER
1615	14

DATE MAILED: 04/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/812,884	Applicant(s) MUMPER ET AL.	
	Examin r Micah-Paul Young	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5,12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Acknowledgment of Papers Received: Election and Restriction Response filed 1/29/03.

Information Disclosure Statement filed 2/5/03.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1- 11, drawn to a stable alcohol-in-fluorocarbon micro-emulsion, classified in class 424, subclass 9.1.

   II. Claims 12 – 20, drawn to a stable liquid hydrocarbon-in-fluorocarbon, classified in class 424, subclass 130.1.

   III. Claims 21 - 33, drawn to nanoparticles composition, classified in class 424, subclass 489.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I, II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, group I is drawn to an alcohol-in-fluorocarbon micro-emulsion, while group II is drawn to a hydrocarbon-in-fluorocarbon and requires specific temperature ranges fro its preparation. Group III however is drawn to a nanoparticle composition. The compounds of groups I and I are silent to the particle size of their respective compounds.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

4. This application contains claims directed to the following patentably distinct species of the claimed invention: in group I, claim 2: a) a drug molecule, b) a food, c) a magnet, d) a sensor molecule; of these species, if a drug molecule is selected, in claim 7: a) plasmid DNA b) oligonucleotide, c) peptide, d) protein, e) antibody, f) small drug molecule, g) rare-earth molecule, claim 9: a) asialofetuin, b) mannan, c) mannose, d) folate, e) a saccharide, f) an antibody. In group II, claim 18: a) asialofetuin, b) mannan, c) mannose, d) folate, e) a saccharide, f) an antibody. In group III, claim 30: a) a drug molecule, b) a food, c) a magnet, d) a sensor molecule; and claim 33: a) an antibody, b) carbohydrate, c) peptide, d) protein.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant has chosen group III and the species of claim 33.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21, 27, and 30 – 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Liversidge et al (USPN 5,145,684),Unger et al (USPN 5,542,935), and (USPN 5,213,788). The claims are drawn to a nanoparticle comprising a liquid component, a surfactant and a molecule of interest. The molecule of interest is a drug molecule.

Liversidge et al discloses claims 21, 27, and 30. The reference teaches a nanoparticle formulation comprising a drug of interest coated with a surfactant. The liquid component of the composition is preferably water (col. 3, lin. 52 – col. 4, lin. 50). The nanoparticles of Liversidge are coated with a surfactant such as polyoxyethylene alkyl esters and polyoxyethylene sorbitan fatty acids *Id.* Also the particles are much less than 400 nm in diameter. These disclosures render, among other render the claims anticipated.

Unger et al discloses claims 21, 27, 31 and 33. The reference discloses a nanoparticle formulation comprising plasmid DNA, surfactants and liquid components (col. 23, lin. 8 – 40; col. 26, lin. 1 – 18). The particles also can be coated with various substances including starches, in order to not trigger the body's immune response (col. 19, lin. 40 –50). The surfactants of the reference are well known in the art such as polyoxyethylene stearate and other ethers. These disclosures along with other render the claims anticipated.

Ranney discloses claims 21, 27 and 32. The reference discloses a nanoparticle composition comprising Gadolinium, surfactants, and other liquid components. The surfactants are well known in the art, and include polyoxyethylene sorbitan esters (col. 2, lin. 38 – 44; col. 19, lin. 29 – 37; col. 20, lin. 34 – 44, lin. 56 – 68; col. 21, lin 7 – 12). These disclosures among other render the claims anticipated.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 22-26, and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al (USPN 5,510,118) and Agostiano, A et al (Micron, 31:253-258, 2000). The claims are drawn to a nanoparticle composition comprising a surfactant or co-surfactant, a molecule of interest, and a liquid component. The claims recite concentrations and ranges for the specific components of the formulation.

Bosh et al discloses a nanoparticle formulation. The formulation comprises surfactants such as polyoxyethylene sorbitan and other ethers (col. 5, lin. 45 – col. 6, lin. 54). The particles of the invention are produced by microfluidization and/or sonication (col. 7, lin. 39 – col. 8, lin. 40).

Agostiano et al teaches a nanoparticle formulation produced from a water-in-oil microemulsion. The formulation comprises synthetic surfactants, and other liquid components. Unstable organic substances were used as molecules of interest (Abstract). The particle sizes were well below 400 nm (Results and Discussion, pg. 255-257).

What the references are lacking are the specific concentrations as recited by applicant. However it is the position of the examiner that these ranges represent simple optimization of the ranges, all of which can be determined through routine experimentation through one of ordinary skill in the art. It has been found that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredients. However, the preparation of various pharmaceutical compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

With regard to applicant limitations to the oil-in-water microemulsion precursor, it is the position of the examiner that these limitations represent product-by-process process claims. The claims are drawn a nanoparticle, a product, yet limitations to the process by which the nanoparticle are made are claimed. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the

product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

Bosh and Agostiano present nanoparticle formulations from oil-in-water and water-in-oil emulsions, comprising liquid components, molecules of interest and surfactants. The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. See *In re Fessmann*, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. See *In re Marosi*, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir.1983)

With this in mind one of ordinary skill in the art would have been motivated to modify either of the reference sin order to optimize the delivery of the particular drugs being delivered. A skilled artisan would have followed the suggestions of Bosch or Agostiano in order to deliver a more bioavailable treatment. It would have been obvious to a skilled artisan to follow these suggestions with an expected result of a nanoparticle with improved stability and bioavailability.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 703-308-7005. The examiner can normally be reached on M-F 7:30am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-7648 for regular communications and 703-746-7648 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Micah-Paul Young
Examiner
Art Unit 1615

MP Young
April 21, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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